



## Efficacy of AQUI-S®: Group Sedation vs. Individual Sedation

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**The drug sponsor has discontinued all activities in pursuit of an FDA approval for AQUI-S®.**

AQUI-S® (50% isoeugenol) is a candidate for U.S. Food and Drug Administration Center for Veterinary Medicine (CVM) approval for use as a zero-withdrawal anesthetic in aquaculture and fisheries management to *sedate all freshwater finfish for management and handling purposes*. As such, fish treated with AQUI-S® could be stocked, released, or harvested immediately following recovery from treatment.

The U.S. Fish & Wildlife Service's Aquatic Animal Drug Approval Partnership program has been actively participating in the AQUI-S® approval process. For example, we have conducted two target animal safety studies and numerous efficacy studies to be included in a New Animal Drug Application (NADA) in support of the drug's U. S. approval. In nearly all of our AQUI-S® efficacy studies, and as per CVM guidance, test fish were individually sedated to "handleable" (herein defined as a fish that has lost equilibrium, stopped swimming, lost reactivity to external stimuli except for strong pressure, and is easily hand-captured, held above the water surface, and measured for length). However, it is common practice in both aquaculture and fisheries management to sedate fish in small groups (e.g., 5 – 20 fish per group). Therefore, in 2005, we conducted three AQUI-S® efficacy studies to investigate if time to handleable was similar between group-sedated and individually sedated fish.

### Methods

All three studies were conducted at 20 mg/L AQUI-S® (currently, the lowest efficacious concentration proposed for the product label). **Study 1** was conducted on rainbow trout *Oncorhynchus mykiss* fingerlings (mean length ~4 cm, water temperature ~12°C). **Study 2** was conducted on channel catfish *Ictalurus punctatus* juveniles (mean length ~22 cm, water temperature ~25°C). **Study 3** was conducted on walleye *Sander vitreus* fingerlings (mean length ~6 cm, water temperature ~22°C).

In each study, test fish were either sedated to handleable as part of a group (Treatment 1) or individually (Treatment 2). Each replicate (N = 3 or 4) of group-sedated fish consisted of simultaneously placing 10 fish into a single container of 20 mg/L AQUI-S® and timing each fish to handleable. Each "replicate" of individually sedated fish consisted of placing a single test fish

into each of 10 containers of 20 mg/L AQUI-S® and timing each fish to handleable. For each group sedated and individually sedated replicate, median time to handleable (to the nearest 0.1 min) was determined [(5<sup>th</sup> longest time + 6<sup>th</sup> longest time) ÷ 2; n = 10 fish] and used as the primary response variable. Subsequently, "average median time to handleable" was calculated for group sedated treatments and individually sedated treatments (sum of median time for all replicates ÷ number of replicates). Average median time-to-handleable values were used to make qualitative comparisons between group-sedated and individually sedated fish. Also, in each study, water temperature, dissolved oxygen concentration, and pH of the AQUI-S® solution in each container was measured once (Table 1).

### Results

In all three studies, there appeared to be little substantive difference in average median time to handleable between group-sedated and individually sedated fish (Tables 2 – 4). In two studies (rainbow trout and channel catfish), average median time to handleable for group-sedated fish was slightly greater (range, 0.3 – 0.5 min) than average median time to handleable for individually sedated fish. In the other study (walleye), average median time to handleable for group-sedated fish was slightly less (0.1 min) than that for individually sedated fish. No mortality or adverse effects were observed during any of the three studies.

### Discussion

Overall, the time to handleable data generated in all three studies suggest that (given a sufficient volume of AQUI-S® solution relative to fish number and size) there is no "group effect" that substantively alters the time required to sedate a fish to handleable. Study results, which were summarized in detailed Final Study Reports, were submitted to and accepted by CVM's Aquaculture Team. As such, the individually sedated time-to-handleable data generated in numerous other AQUI-S® efficacy studies should be representative of real-world scenarios in which fish are sedated to handleable in small groups.

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**Table 1.** Mean length of test fish and water quality conditions under which test fish were sedated to handleable at 20 mg/L AQUI-S®.

Study	Mean length (cm)	Mean water temperature (°C)	Mean dissolved oxygen concentration (mg/L)	Mean pH
<b>Individually sedated</b>				
1 (RBT)	4.3	12.2	8.0	7.96
2 (CCF)	22.0	25.1	6.3	nc*
3 (WAE)	6.1	21.7	8.4	8.33
<b>Group-sedated</b>				
1 (RBT)	4.4	12.5	7.9	7.95
2 (CCF)	22.5	24.9	6.2	nc
3 (WAE)	6.1	21.7	8.5	8.32
<b>Footnote:</b> * = not collected				

**Table 3.** Study 2 - Median time to handleable for channel catfish (mean length, 22.4 cm) group-sedated or individually sedated at 20 mg/L AQUI-S® (water temperature, 25°C).

Replicate	Median time to handleable (min)	
	Group sedation	Individual sedation
1	7.1	6.4
2	6.7	5.5
3	5.1	5.6
<b>Average median time</b>	<b>6.3</b>	<b>5.8</b>

**Table 2.** Study 1 - Median time to handleable for rainbow trout (mean length, 4.3 cm) group-sedated or individually sedated at 20 mg/L AQUI-S® (water temperature, 12°C).

Replicate	Median time to handleable (min)	
	Group sedation	Individual sedation
1	5.2	4.8
2	4.7	4.9
3	4.9	4.8
4	5.9	5.2
<b>Average median time</b>	<b>5.2</b>	<b>4.9</b>

**Table 4.** Study 3 - Median time to handleable for walleye (mean length, 6.1 cm) group-sedated or individually sedated at 20 mg/L AQUI-S® (water temperature, 22°C).

Replicate	Median time to handleable (min)	
	Group sedation	Individual sedation
1	5.9	5.3
2	5.1	6.2
3	6.1	5.9
<b>Average median time</b>	<b>5.7</b>	<b>5.8</b>